PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

(Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference WO 826	**FOR FURTHER ACTION**	See Form PCT/IPEA/416
International application No. PCT/EP2004/051625	International filing date *(day/month/year)* 27.07.2004	Priority date *(day/month/year)* 28.07.2003
International Patent Classification (IPC) or national classification and IPC A61K31/427, A61P37/00, A61P29/00, C07D417/06, C07D417/14		
Applicant APPLIED RESEARCH SYSTEMS ARS HOLDING N.V. et al.		

1. This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36.
2. This REPORT consists of a total of 6 sheets, including this cover sheet.
3. This report is also accompanied by ANNEXES, comprising:
   a. ☒ *sent to the applicant and to the International Bureau)* a total of 1 sheets, as follows:
      ☒ sheets of the description, claims and/or drawings which have been amended and are the basis of this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions).
      ☐ sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. I and the Supplemental Box.
   b. ☐ *(sent to the International Bureau only)* a total of (indicate type and number of electronic carrier(s)) , containing a sequence listing and/or tables related thereto, in computer readable form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions).

4. This report contains indications relating to the following items:

☒	Box No. I	Basis of the opinion
☐	Box No. II	Priority
☒	Box No. III	Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
☐	Box No. IV	Lack of unity of invention
☒	Box No. V	Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
☐	Box No. VI	Certain documents cited
☐	Box No. VII	Certain defects in the international application
☐	Box No. VIII	Certain observations on the international application

Date of submission of the demand	Date of completion of this report
04.04.2005	29.09.2005
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INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.
PCT/EP2004/051625

Box No. I Basis of the report

1. With regard to the **language**, this report is based on the international application in the language in which it was filed, unless otherwise indicated under this item.

   ☐ This report is based on translations from the original language into the following language , which is the language of a translation furnished for the purposes of:
   - ☐ international search (under Rules 12.3 and 23.1(b))
   - ☐ publication of the international application (under Rule 12.4)
   - ☐ international preliminary examination (under Rules 55.2 and/or 55.3)

2. With regard to the **elements*** of the international application, this report is based on *(replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report)*:

Description, Pages

1-59	as originally filed

Claims, Numbers

1-11, 12 (part), 14 (part), 15-22	as originally filed
12 (part), 13, 14 (part)	as amended (together with any statement) under Art. 19 PCT

☐ a sequence listing and/or any related table(s) - see Supplemental Box Relating to Sequence Listing

3. ☐ The amendments have resulted in the cancellation of:
   - ☐ the description, pages
   - ☐ the claims, Nos.
   - ☐ the drawings, sheets/figs
   - ☐ the sequence listing *(specify)*:
   - ☐ any table(s) related to sequence listing *(specify)*:

4. ☐ This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).
   - ☐ the description, pages
   - ☐ the claims, Nos.
   - ☐ the drawings, sheets/figs
   - ☐ the sequence listing *(specify)*:
   - ☐ any table(s) related to sequence listing *(specify)*:

* *If item 4 applies, some or all of these sheets may be marked "superseded."*

Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application,

☒ claims Nos. 1,11,12 (all part)

because:

☐ the said international application, or the said claims Nos. relate to the following subject matter which does not require an international preliminary examination (specify):

☒ the description, claims or drawings *(indicate particular elements below)* or said claims Nos. 1,11,12 (all part) are so unclear that no meaningful opinion could be formed *(specify)*:

see separate sheet

☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

☐ no international search report has been established for the said claims Nos.

☐ the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:

the written form	☐	has not been furnished
	☐	does not comply with the standard
the computer readable form	☐	has not been furnished
	☐	does not comply with the standard

☐ the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-*bis* of the Administrative Instructions.

☐ See separate sheet for further details

Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	6-8, 10, 12, 13, 15-20, 22
	No:	Claims	1-5, 9, 11, 14, 21
Inventive step (IS)	Yes:	Claims	6-8, 10, 12, 13, 15-20
	No:	Claims	1-5, 9, 11, 14, 21, 22
Industrial applicability (IA)	Yes:	Claims	1-22
	No:	Claims	

2. Citations and explanations (Rule 70.7):

see separate sheet

III. Non-establishment of opinion

In the definitions of R^1, R^2 and R^3 in claims 1, 11 and 12 these substituents are described as "comprising or consisting of" various groups. If these substituents comprise the given groups, this implies that they may contain any other undefined group in addition to the comprised group. The scope of the claims is therefore not clear and they do not fulfil the requirements of Article 6 PCT. The search has only been performed for the compounds of formula (I) wherein R^1, R^2 and R^3 consist of the defined groups as this part of the claim is clear. The following examination is also based on this clear subject matter only.

It is noted that the last excluded compound of claims 1 and 11 does not fall within the scope of formula (I) because of the position of attachment of the naphthyl group to the alkylidene group. This being the case, there is a contradiction in claim 1 which could lead to doubt as to the intended scope of protection. For this reason claims 1 and 11 do not fulfil the requirements of Article 6 PCT.

V. Reasoned statement

Reference is made to the following documents:
D1: EP-A-0 697 410
D2: Roué et al., Tetrahedron 55 (1999) 14729-14738

Novelty

D1 discloses a general formula (I) overlapping with present formula (I). The specific examples of D1 have been excluded by proviso from claim 1. However, in such a case, it is not sufficient to delete only the examples in order to establish novelty - the whole area of overlap must be removed. The compounds of D1 are described as being useful in the treatment of i.a. kidney diseases. Claims 1-5, 9, 11, 14 and 21 are anticipated by D1.

D2, example 10 has been excluded from claim 1 by proviso.

Claims 1-5, 9, 11, 14 and 21 do not fulfil the requirements of Article 33(2) PCT.

Inventive step

In view of their lack of novelty, claims 1-5, 9, 11, 14 and 21 cannot be considered inventive.

Re. claims 6-8, 10, 12, 13, 15-20 and 22:
The technical problem underlying the present application appears to be the provision of compounds active against one or more of a wide variety of diseases specified in claim 12, for example kidney diseases. The compounds of claims 6-8 differ from the compounds of D1 because they lack the cyano N-substituent. It would not have been obvious, using the cited documents, to replace the cyano group by one of the groups claimed in claims 6-8 in the expectation that the activity would be maintained. Therefore those compounds of claims 6-8 which have the alleged activity may be considered inventive. The compounds of claim 10 differ from those of D1 either for the same reason as those of claims 6-8 or because of the identity of the bicyclic group (quinoxaline instead of naphthyl or benzodioxole). In the absence of any document suggesting the equivalence of these bicyclic rings in compounds with the same activity, the compounds of claim 10 may be considered inventive, insofar as they have the alleged activity. Claims 12, 13, 15-20 concern 2nd medical uses wherein none of the listed diseases overlap with those listed in D1. It would not have been obvious that compounds having the activities listed in D1 would also have the activities listed in these claims. Claims 15-20 may therefore be considered inventive. The method of claim 22 is considered to be a routine method for preparing the desired compounds, and is thus only inventive insofar as the final products of this process are new and inventive.

Claims 1-5, 9, 11, 14, 21 and 22 do not fulfil the requirements of Article 33(3) PCT.

Industrial applicability
Claims 1-22 fulfil the requirements of Article 33(4) PCT.

R^1 is selected from the group comprising or consisting of H, CN, carboxy, acyl, C_1-C_6-alkoxy, halogen, hydroxy, acyloxy, C_1-C_6-alkyl carboxy, C_1-C_6-alkyl acyloxy, C_1-C_6-alkyl alkoxy, alkoxycarbonyl, C_1-C_6-alkyl alkoxycarbonyl, aminocarbonyl, C_1-C_6-alkyl aminocarbonyl, acylamino, C_1-C_6-alkyl acylamino, ureido, C_1-C_6-alkyl ureido, amino, C_1-C_6-alkyl amino, ammonium, sulfonyloxy, C_1-C_6-alkyl sulfonyloxy, sulfonyl, C_1-C_6-alkyl sulfonyl, sulfinyl, C_1-C_6-alkyl sulfinyl, sulfanyl, C_1-C_6-alkyl sulfanyl, sulfonylamino, C_1-C_6-alkyl sulfonylamino or carbamate;
R^2 is selected from the group comprising or consisting of H, halogen, acyl, amino, C_1-C_6-alkyl, C_2-C_6-alkenyl, C_2-C_6-alkynyl, C_1-C_6-alkyl carboxy, C_1-C_6-alkyl acyl, C_1-C_6-alkyl alkoxycarbonyl, C_1-C_6-alkyl aminocarbonyl, C_1-C_6-alkyl acyloxy, C_1-C_6-alkyl acylamino, C_1-C_6-alkyl ureido, C_1-C_6-alkyl carbamate, C_1-C_6-alkyl amino, C_1-C_6-alkyl alkoxy, C_1-C_6-alkyl sulfanyl, C_1-C_6-alkyl sulfinyl, C_1-C_6-alkyl sulfonyl, C_1-C_6-alkyl sulfonylaminoaryl, aryl, heteroaryl, C_3-C_8-cycloalkyl or heterocycloalkyl, C_1-C_6-alkyl aryl, C_1-C_6-alkyl heteroaryl, C_2-C_6-alkenyl-aryl or -heteroaryl, C_2-C_6-alkynyl aryl or -heteroaryl, carboxy, cyano, hydroxy, C_1-C_6-alkoxy, nitro, acylamino, ureido, sulfonylamino, sulfanyl, or sulfonyl;
G is a C_1-C_6-alkyl, C_2-C_6-alkyenyl, C_2-C_6-alkynyl, heteroaryl, C_1-C_6-alkyl aryl, C_1-C_6-alkyl heteroaryl, C_2-C_6-alkenyl-aryl or -heteroaryl, C_2-C_6-alkynyl aryl or -heteroaryl, C_1-C_6-alkoxy, cyano, C_1-C_6-acyl, or a sulfonyl moiety;
R^3 is selected from the group comprising or consisting of H or C_1-C_6-alkyl; for the preparation of a medicament for the prophylaxis and/or treatment of autoimmune disorders and/or inflammatory diseases, cardiovascular diseases, neurodegenerative diseases, ~~kidney diseases~~, platelet aggregation, cancer, transplantation, graft rejection or lung injuries.

13. Use according to claim 12, wherein G is a C_1-C_6-alkoxy, cyano or a sulfonyl moiety.

14. Use according to any claims 11 to 13 wherein the imino-azolinone-vinyl fused-benzene derivative is selected from the group consisting of: